SUMMARY

Characterization of a non selective cation channel in ovine rumen epithelium cells

Implications on the osmoregulation of the rumen fluid

Depending on the diet, characteristic changes appear in the rumen fluid of sheep and cows. The rise in SCFA concentration and the reduction in pH as well as their possible pathological implications have been known for many years and have been intensively studied. The changes induced by the diet cause a reduction of feed intake, a drop in saliva production, a decrease in fermentation and damage to the functions of the epithelium. While the mechanisms regulating pH have been extensively examined, there is only descriptive data concerning the factors that influence osmotic pressure.

It was the aim of this study to characterize a mechanism of osmoregulation in the rumen fluid. It has been known for many years that an increase in sodium absorption, which is probably caused by the opening of a non-selective cation channel, causes adequate osmoregulation in reaction to an elevated potassium concentration in the rumen. This unique mechanism is responsible for the fact that the sum of the cations sodium and potassium remains largely constant in the ruminal fluid. Therefore, the experiments performed in this study pursued the aim of a further characterization of this cation channel using the patch clamp technique.
Various preceding studies portended that - in analogy to the kidney - the regulation of sodium resorption is subject to a complex hormonal regulation. The endogenous production of prostaglandins is well documented. However, there is no clear data on the effect of prostaglandins on electrogenic sodium resorption so far.

The examinations using isolated rumen epithelium cells yielded the following results:

- The electrogenic sodium conductance could be elevated by elevation of cytosolic cAMP in the presence of physiological amounts of calcium and magnesium. Under these conditions, the inward current of cells filled with choline chloride rose from 100 ± 7 % to 236 ± 26 % ($p < 0,001$) with a marked depolarization from 10 ± 2 mV to 28 ± 3 mV ($p < 0,001$) (choline chloride without cAMP: n = 23; choline chloride with cAMP: n = 19).
- A pharmacological increase of cytosolic cAMP by PGE_2 and forskolin had comparable effects to the direct application of cAMP via the pipette solution. Theophylline had no significant effect, probably due to the lack of prostaglandin synthesis of the isolated cells.
- The stimulation of electrogenic sodium conductance with a marked rise in reversal potential only occurred in the presence of cytosolic magnesium and can therefore presumably not be explained fully by the decrease of the cytosolic magnesium concentration induced by the stimulation of the Na^+/Mg^{2+}-exchanger.
- The electrogenic cation conductance of the membrane was unspecific. The conductance sequence of $K^+ > Cs^+ > Na^+$ was calculated from the reversal potentials, and corresponds to an Eisenmann-sequence III or IV. Thus, ions probably permeate the channel only after losing their hydration shell.
- The electrogenic sodium conductance could be stimulated by removal of divalent cations and blocked by verapamil. In contrast, amiloride had no effect.
- Elevation of extracellular magnesium concentration to 65 mM provided no evidence for a conductance of this ion.
- A substantial electrogenic conductance for chloride was also demonstrated.

These results demonstrate that sodium resorption is facilitated by a non selective cation channel, the conductance of which is increased by prostaglandins. Apparently, cAMP interacts directly with the channel.

Key words:
osmoregulation, cations, cation channels, ion-transport, Sodium, rumen, sheep